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(54) Title: GENETICALLY MODIFIED NON-HUMAN MAMMALS AND CELLS

(57) Abstract: A genetically modified non-human mammal or cell characterised in that it does not comprise a nucleic acid sequence which itself encodes any endogenous immunoglobulin heavy chain constant region locus polypeptide.

International Application No PCT/GB2004/000768 A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12P21/08 C12N C12N5/16 C12N15/85 C12N15/13 A01K67/027 C07K16/00 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, BIOSIS, EMBASE, WPI Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Category ° Relevant to claim No. X WO 98/54348 A (BRUGGEMANN MARIANNE ; 1-6,11, BABRAHAM INST (GB)) 16-22. 3 December 1998 (1998-12-03) 29-33, 39-47, Υ the whole document, in particular Example 57-70 7-10. 1 and claim 7 12-15. 23-28. 34-38, 48~56 Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance earlier document but published on or after the international invention filing date *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled document referring to an oral disclosure, use, exhibition or document published prior to the international filing date but later than the priority date claimed *&* document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 18 August 2004 24/08/2004 Name and mailing address of the ISA

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	C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT Category Citation of document, with indication, where appropriate and the continuation of document.					
	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.				
Υ	ZOU YONG-RUI ET AL: "Cre-loxP-mediated gene replacement: A mouse strain producing humanized antibodies" CURRENT BIOLOGY, vol. 4, no. 12, 1994, pages 1099-1103, XP009034794 ISSN: 0960-9822 cited in the application the whole document	7-10, 12-15, 23-28, 34-38, 48-56				
A	WO 90/04036 A (AGRICULTURAL & FOOD RES; BRUGGEMANN MARIANNE (GB); MEDICAL RES COUNCI) 19 April 1990 (1990-04-19) cited in the application					
Α .	METZGER D ET AL: "CONDITIONAL SITE-SPECIFIC RECOMBINATION IN MAMMALIAN CELLS USING A LIGAND-DEPENDENT CHIMERIC CRE RECOMBINASE" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 92, no. 15, 18 July 1995 (1995-07-18), pages 6991-6995, XP000615550 ISSN: 0027-8424					
4	JAKOBOVITS A ET AL: "ANALYSIS OF HOMOZYGOUS MUTANT CHIMERIC MICE: DELETION OF THE IMMUNOGLOBULIN HEAVY-CHAIN JOINING REGION BLOCKS B-CELL DEVELOPMENTAND ANTIBODY PRODUCTION" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 90, no. 6, 1 March 1993 (1993-03-01), pages 2551-2555, XP000673147 ISSN: 0027-8424 cited in the application					
,Х	US 6 570 061 B1 (RAJEWSKY KLAUS ET AL) 27 May 2003 (2003-05-27) the whole document	1-70				
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International Application No
PCT/GB2004/000768

Category °	ation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where			
	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
P,X	RONAI D ET AL: "Use of a simple, general targeting vector for replacing the DNA of the heavy chain constant region in mouse hybridoma cells" JOURNAL OF IMMUNOLOGICAL METHODS 01 APR 2003 NETHERLANDS, vol. 275, no. 1-2, 1 April 2003 (2003-04-01), pages 191-202, XP004416768 ISSN: 0022-1759	1-6,11, 16-22, 29-33, 39-47, 57-70		
P,Y	the whole document	7-10, 12-15, 23-28, 34-38, 48-56		
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Information on patent family members

International Application No
PCT/GB2004/000768

Patent document	T			1017	GB2004/000768
cited in search report		Publication date		Patent family member(s)	Publication date
WO 9854348	A 	03-12-1998	AU WO	7667698 A 9854348 A1	30-12-1998 03-12-1998
WO 9004036	A	19-04-1990	AT AU DE DE EP WO JP JP KR US	138104 T 4417389 A 68926508 D1 68926508 T2 0438474 A1 9004036 A1 4500911 T 3484442 B2 2003192699 A 164608 B1 5545807 A	15-06-1996 01-05-1990 20-06-1996 31-10-1996 31-07-1991 19-04-1990 20-02-1992 06-01-2004 09-07-2003 15-01-1999 13-08-1996
US 6570061	B1	27-05-2003	DE WO EP JP US	4228162 C1 9404667 A1 0658197 A1 8504564 T 2003167489 A1	13-01-1994 03-03-1994 21-06-1995 21-05-1996 04-09-2003